Overview of FDA review of Multiplexed/IVDMIA Devices

FDA Public Workshop - LC/MS in the Clinic

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Multiplex Test Systems

- 21 CFR 862.2570, Class II
- Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems - Guidance for Industry and FDA Staff

Multiplex Test Systems

"This type of device is intended to measure and sort multiple signals generated by an assay from a clinical sample. This instrumentation is used with a specific assay to measure multiple similar analytes that establish a single indicator to aid in diagnosis. Such instrumentation may be compatible with more than one specific assay."

FDA Cleared Multiplex Test Systems

- Affymetrix GeneChip Microarray Instrumentation system + Roche Amplichip
- NMR LipoProfile test on the Vantera Clinical Analyzer
- Verigene® Respiratory Virus Nucleic Acid Test on the Verigene System
- SQI Ig_plex Celiac DGP Panel on the sqid-X system

Performance studies

- Reproducibility at 3 sites
  - Assess overall instrumentation performance, e.g., sample processing consistency, scanner drift
- Method comparison/accuracy
- Interference
- Linearity
- Limits of detection
- Each analyte is individually validated

Lessons Learned - Multiplex

- Don’t modify the device once you start validation
- Focus on carryover and/or interference of one analyte on the other (especially high levels)
  - If adding a new analyte to a multiplex test system, a risk analysis could be used to inform what studies should be performed for modified device
- Pre-analytical variables can be very important to control

In Vitro Diagnostic Multivariate Index Assays (IVDMIAs)

IVDMIA is a device that combines the values of multiple variables using an interpretation function to yield a single, patient-specific result (e.g., a “classification,” “score,” “index,” etc.), that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease.

FDA Cleared IVDMIAs

- Mammaprint
- AlloMap
- Ova1, OVA NG, Risk of Ovarian Malignancy Algorithm (ROMA™)
- Nephrocheck

Lessons Learned - IVDMIAs

- Keep discovery and validation set separate
- If the populations of the discovery and validation sets are different, the IVDMIA may not work as predicted
- Don’t modify the device once you start validation
- Make sure the validation population reflects the Intended Use of the device
- Evaluate the robustness of the algorithm given the imprecision of the separate analytes/components/lot

FDA Guidance Documents

- Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems - Guidance for Industry and FDA Staff
- Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests
- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices etc.
- Requests for Feedback on Medical Device Submissions: the Pre-Submission Program and Meetings with Food and Drug Administration Staff

We also recommend the Clinical Laboratory and Standards Institute Evaluation Protocol Guidelines

Thank you!

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